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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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ADVENTIS PHARMACEUTICALS INC
Route 202-206
PO Box 6800
Bridgewater, NJ 08807

EXAMINER
STEADMAN, DAVID J

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 01/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/084,814	SLIJKHUIS ET AL.	
	Examiner	Art Unit	
	David J Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20,34,36-42 and 44-46* is/are pending in the application.

4a) Of the above claim(s) *20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34,36-42 and 44-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 February 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 07/474,798.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] Claims 20, 34, 36-42, and 44-46 are pending in the application.

[2] Applicants' amendment to the claims, filed December 17, 2004, is acknowledged.

This listing of the claims replaces all prior versions and listings of the claims.

[3] It is noted that claim 20 is withdrawn from consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim, however, the status identifier of the claim fails to properly identify the claim as "withdrawn." Applicants are advised to properly identify claims by status identifier according to 37 CFR 1.121.

[4] Applicants' amendment to the specification and abstract, filed December 17, 2004, is acknowledged.

[5] Applicant's arguments filed December 17, 2004 have been fully considered and are deemed to be persuasive to overcome some of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[6] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Priority

[7] Applicants dispute the examiner's assertion that the instant application does not receive the benefit of priority under 35 USC 119(a)-(d) to applications Netherlands

88202080.3, filed 09/23/88 and Netherlands 88200904.6, filed 05/06/88. Applicants assert the instant application properly claims foreign priority to applications Netherlands 88202080.3 and Netherlands 88200904.6 through PCT/NL89/00032, to which the instant application claims priority.

Applicants' argument is not found persuasive. The instant application claims *foreign* priority to PCT/NL89/00032, not domestic priority. Therefore, as the earliest US non-provisional application was filed more than one year after the filing date of applications Netherlands 88202080.3 and Netherlands 88200904, the instant application receives only the benefit of foreign priority to application PCT/NL89/00032.

Sequence Compliance

[8] This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825; applicants' attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). To be in compliance, applicants should identify nucleotide sequences of at least 10 nucleotides and amino acid sequences of at least 4 amino acids in the specification by a proper sequence identifier, i.e., "SEQ ID NO:" (see MPEP 2422.01). If these sequences have not been listed in the computer readable form and paper copy of the sequence listing, applicant must provide an initial computer readable form (CRF) copy of the "Sequence Listing", an initial paper copy of the "Sequence Listing", as well as an amendment

directing its entry into the specification, and a statement that the content of the paper and CRF copies are the same and, where applicable, include no new matter as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d). See particularly Figures 3, 5, 7, 13, 18, 20, 23, 25, 29, 33, 36-38, and 40.

Specification/Informalities

[9] The objection to the specification is maintained for the reasons of record and the reasons stated below. The amendment to the specification, filed December 17, 2004, indicates that application 08/054,185 is a continuation of *two different applications*. It is suggested that applicants correctly state the priority claim to prior applications in the first paragraph of the specification.

[10] The specification is objected to as some text at the bottom of the pages of the substitute specification, filed December 17, 2004, is illegible. Also, the examiner requests that applicants increase the font size of the text as it is difficult to read due to its small size.

[11] RESPONSE TO ARGUMENT: Applicants argue the objections to the specification have been overcome by amendment. However, for the reasons stated above, the amendment does not overcome the objections.

Claim Objections

[12] Claim 38 is objected to as being grammatically incorrect in the recitation of "wherein second" and should be replaced with, for example, "wherein the second."

[13] Claim 41 is objected to as being grammatically incorrect in the recitation of "or Bacillus or Escherichia coli" and should be replaced with, for example, "Bacillus or Escherichia coli."

Claim Rejections - 35 USC § 112, First Paragraph

[14] The written description rejection of claims 34, 36-42, and 44-46 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The examiner maintains the position that the representative disclosed species of expression vectors fails to adequately describe all species encompassed by the claims.

RESPONSE TO ARGUMENT: Applicants argue the "claims are limited to expression cassettes comprising heterologous DNAs of specific enzymes selected from a limited number of species." Applicants argue the specification allegedly teaches the sources of the enzymes, allegedly contains "many examples of these heterologous DNAs from several species," and allegedly teaches a method of obtaining a heterologous DNA used in the instant invention for that alleged "limited number of species."

Applicants' argument is not found persuasive. As an initial matter, it is noted that applicants refer to ¶¶ 0092-0105 in their argument. However, there is no numbering of paragraphs in the substitute specifications or in the original specification. It appears applicants are referring to the corresponding published patent application, US 20030108982. References to ¶¶ 0092-0105 have been interpreted accordingly.

Addressing the merits of applicants' argument, as stated in a previous Office action, "[t]he CAFC in *UC California v. Eli Lilly*, (43 USPQ2d 1398) stated that: 'In claims to genetic material, however a generic statement such as "vertebrate insulin cDNA' or 'mammalian insulin cDNA', without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus.' Similarly with the claimed genus of expression cassettes, the functional definition of the genus does not provide any structural information commonly possessed by members of the genus which distinguish the heterologous DNA(s) of the expression cassettes from other heterologous DNA(s) such that one can visualize or recognize the identity of the members of the genus." In this case, the claims recite merely functional features of the recited genus of heterologous DNAs and fail to distinguish the genus of by any structural characteristics and there is no disclosed correlation between the function and the structure of the recited DNAs such that a skilled artisan could visualize all members of the genus based on mere recitation of the function of the genus. The recited genus of DNAs encompasses species that have not been described in the specification/prior art as the recited genus reads on, *e.g.*, allelic variants that have not been disclosed in the specification or prior art and mutants and variants of known species and those yet to be isolated. It should be noted that the species encompassed

by the genus are not limited to those disclosed in the specification. While it is acknowledged that the specification discloses the following representative species of the recited genus of expression vectors: pGBSCC-1, -2, -3, -4, -5, -6, -7, -8, -9, -10, -11, -12, -13, -14, -15, -16, and –17; pGB17alpha-1, -2, -3, -4, and –5; pGBC21-1, -2, -3, -4, -5, -6, -7, -8, and –9; and pGB11beta-1, -2, -3, and –4, these representative examples fail to describe all members of the genus as encompassed by the claims. Furthermore, it is noted that the genera of heterologous DNAs is limited to those encoding bovine, human, *P. testosteroni, S. griseocarneus, B. sterolicum, C. lunata, or C. blakesleeana.* MPEP § 2163 states (citing *Amgen*, 927 F.2d at 1206, 18 USPQ2d at 1021), "A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials." The specification fails to convey the common distinguishing characteristics of a DNA that encodes a recited enzyme that is considered to be a bovine, human, *P. testosteroni, S. griseocarneus, B. sterolicum, C. lunata, or C. blakesleeana* such that one can visualize the members of the genus and distinguish a subgenus of bovine, human, *P. testosteroni, S. griseocarneus, B. sterolicum, C. lunata, or C. blakesleeana* enzymes from the broader genus of enzymes that is not of bovine, human, *P. testosteroni, S. griseocarneus, B. sterolicum, C. lunata, or C. blakesleeana* origin. As such, it is the examiner's position that the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

[15] The scope of enablement rejection of claims 34, 36-42, and 44-46 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The examiner maintains the position that the specification, while being enabling for the expression vectors pGBSCC-1, -2, -3, -4, -5, -6, -7, -8, -9, -10, -11, -12, -13, -14, -15, -16, and –17; pGB17alpha-1, -2, -3, -4, and –5; pGBC21-1, -2, -3, -4, -5, -6, -7, -8, and –9; and pGB11beta-1, -2, -3, and –4, does not reasonably enable all expression cassettes as broadly encompassed by the claims.

RESPONSE TO ARGUMENT: Applicants argue the "claims are limited to expression cassettes comprising heterologous DNAs of specific enzymes selected from a limited number of species." Applicants argue the specification allegedly teaches the sources of the enzymes, allegedly contains "many examples of these heterologous DNAs from several species," and alleges one of skill in the art would be able to isolate the full scope of heterologous DNAs encompassed by the claims in view of the guidance provided in the specification.

Applicants' argument is not found persuasive. As an initial matter, it is noted that applicants refer to ¶¶ 0092-0105 in their argument. However, there is no numbering of paragraphs in the substitute specifications or in the original specification. It appears applicants are referring to the corresponding published patent application, US 20030108982. References to ¶¶ 0092-0105 have been interpreted accordingly. The examiner reiterates the detailed analysis of the Factors of *In re Wands* as set forth in a previous Office action and incorporated herein. See particularly pp. 10-14 of the Office action mailed June 17, 2004. While the examiner acknowledges disclosure of the

working examples of expression vectors pGBSCC-1, -2, -3, -4, -5, -6, -7, -8, -9, -10, -11, -12, -13, -14, -15, -16, and –17; pGB17alpha-1, -2, -3, -4, and –5; pGBC21-1, -2, -3, -4, -5, -6, -7, -8, and –9; and pGB11beta-1, -2, -3, and –4, these working examples fail to provide the necessary guidance for making all heterologous DNAs as broadly encompassed by the claims, including allelic variants of known DNAs, which may or may not be sufficiently structurally related to the working examples such that they may be identified by known methods, *e.g.*, hybridization, and also includes mutants and variants of known DNAs and DNAs yet to be isolated. Applicants do not dispute the examiner's assertion that there is a high level of unpredictability in altering the sequence of an encoding DNA with an expectation of obtaining a DNA encoding a polypeptide having the desired activity/utility. Further, applicants do not dispute the cited teachings of Branden et al. and Witkowski et al. (pp. 12-13 of the Office action mailed June 17, 2004), providing objective support of such unpredictability. While methods of altering an encoding DNA sequence were known at the time of the invention, *e.g.*, site-directed mutagenesis, it was not routine to screen all variants of a DNA, including DNAs whose sequences were yet to be isolated, to those that encode polypeptides having the desired activity/utility, particularly in view of the lack of guidance regarding those amino acids of the encoded polypeptides that can be altered and still maintain the respective enzymatic activity. Thus, in view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high level of unpredictability as evidenced by the prior art, and the significant amount of experimentation required (all discussed in detail at pp. 10-14 of the Office action mailed

6/17/2004), it is the examiner's position that undue experimentation would be necessary for a skilled artisan to make the entire scope of the claimed invention.

Claim Rejections – Double Patenting

[16] The obviousness-type double patenting rejection of claims 34, 36-37, 39-42, and 44 as being unpatentable over claims 1-7, 13-16, and 21 of US Patent 5,869,283, the obviousness-type double patenting rejection of claims 34, 36-37, 39-42, and 44 as being unpatentable over claims 1-11 of US Patent 6,171,836, and the obviousness-type provisional double patenting rejection of claims 34, 36-37, 39-42, and 44 as being unpatentable over claims 34-43 of co-pending Application No. 10/462,128 are maintained for the reasons of record and the reasons stated below.

RESPONSE TO ARGUMENT: Applicants argue the rejections have been overcome by amendment as, applicants allege, the claims of the US patents or US patent application do not make obvious "the particular requirements of the pending claims for a specific combination of enzymes encoded in an expression cassette."

Applicants' argument is not found persuasive. While the claims of the patents and the co-pending application may not recite the expression cassettes comprising the specific species of DNAs encoding enzymes as recited in the claims of the instant application, these DNAs are specifically disclosed embodiments of the respective US patents (see, *e.g.,* column 7 of US Patent 5,869,283 and column 7 of US Patent 6,171,836) and the co-pending patent application (see, *e.g.,* pp. 19-20 of co-pending Application No. 10/462,128). The claims of the instant application cannot be considered

to be patentably distinct over the claims of the patents or co-pending patent application when there is a specifically disclosed embodiment in the patents or patent application that supports the patent or co-pending patent application claims and falls within the scope of the instant claims because it would have been obvious to one of ordinary skill in the art to modify the claimed expression cassette, host cell, or method by selecting a specifically disclosed embodiment that supports those claims. One of ordinary skill in the art would have been motivated to do this because those embodiments are disclosed as being preferred embodiments within the scope of the patent or co-pending patent application claims.

Claim Rejections - 35 USC § 103

[17] The rejection of claims 34, 36-39, 42, and 44-45 under 35 U.S.C. 103(a) as being unpatentable over Zuber et al. in view of Sedlaczek et al. (Crit Rev Biotechnol 7:187-236) and Bulow et al. is maintained for the reasons of record (item [25] of the Office action mailed June 17, 2004) and the reasons stated below.

RESPONSE TO ARGUMENT: Applicants argue the Office action "fails to state a prima facie case of obviousness, because [the rejection relies] on Sedlaczek et al. (Crit Rev Biotechnol 7:187-236), and Sedlaczek et al. was never evaluated to determine whether it is a proper reference against the instant application." Applicants argue the Office action "contains no allegation or suggestion that Sedlaczek et al. is a proper § 102(b) reference...or a proper § 102(e) reference." Applicants' argument is not found persuasive.

The examiner evaluated and properly applied the reference of Sedlaczek et al. as § 102(b) reference in the instant rejection. MPEP 2141.01 states that prior art available under 35 U.S.C. is available under 35 U.S.C. 103. Thus, the question remains – is the reference of Sedlaczek et al. a reference that is available under 35 U.S.C. 102? According to the MPEP, a reference is available as prior art under 35 U.S.C. 102(b) if "the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States." In this case, the earliest domestic priority date is July 16, 1990, which is the filing date of US non-provisional application 07/474,798. The reference of Sedlaczek et al. was publicly available in 1988, which is at least "more than one year prior to the date of application for patent in the United States." As such, the reference of Sedlaczek et al. was properly evaluated and applied as prior art under 35 U.S.C. 102(b).

Conclusion

[18] Status of the claims:

- Claims 20, 34, 36-42, and 44-46 are pending.
- Claim 20 is withdrawn from consideration.
- Claims 34, 36-42, and 44-46 are rejected.
- No claim is in condition for allowance.

Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be reached Monday-Friday from 7:00 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX number for submission of official papers to Group 1600 is (703) 308-4242. Draft or informal FAX communications should be directed to (703) 746-5078. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

01-19-05

David J. Steadman, Ph.D.
Primary Examiner
Art Unit 1652

DAVID J. STEADMAN, PH.D.
PRIMARY EXAMINER